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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,846	01/26/2001	David P. Hornby	P-582	7859

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	10

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/770,846	Applicant(s) HORNBY ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2002* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Miscellaneous

1. Any rejections not reiterated below are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Mitchell et al (Anal. Biochem. (1989) 178:239-242).

Mitchell teaches a method for separating the complementary single-stranded polynucleotide products of an amplification reaction from one another (page 240, subheading "Generation of ssDNA") comprising:

(a) amplifying a target polynucleotide by PCR using two oligonucleotide primers where one primer comprises a biotin tag (which is negatively charged and comprises hydrophobic moieties), to produce an amplification product where one strand is tagged with biotin and the complementary strand is not tagged with biotin (see page 240, subheading "PCR amplification"),

(b) applying the amplification product mixture to a separation medium, here streptavidin agarose, wherein the biotin chemical tag can interact with the separation medium (see page 240, subheading "generation of ssDNA").

(c) eluting the amplification products from the separation medium by means of a mobile phase, here the NaOH denaturation step, wherein the interaction between the tag and the separation medium results in the physical separation of the tagged amplification product from the non-tagged amplification product (page 240, subheading "Generation of ssDNA").

Mitchell teaches detection of the amplification products (see page 240, figure 1) as well as collection of the amplification products (page 240, subheading "Generation of ssDNA").

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitchell et al (Anal. Biochem. (1989) 178:239-242) in view of Gjerde et al (U.S. Patent 6,265,168).

Mitchell teaches a method for separating the complementary single-stranded polynucleotide products of an amplification reaction from one another (page 240, subheading "Generation of ssDNA") comprising:

(a) amplifying a target polynucleotide by PCR using two oligonucleotide primers where one primer comprises a biotin tag (which is negatively charged), to produce an amplification product where one strand is tagged with biotin and the complementary strand is not tagged with biotin (see page 240, subheading "PCR amplification"),

(b) applying the amplification product mixture to a separation medium, here streptavidin agarose, wherein the biotin chemical tag can interact with the separation medium (see page 240, subheading "generation of ssDNA").

(c) eluting the amplification products from the separation medium by means of a mobile phase, here the NaOH denaturation step, wherein the interaction between the tag and the separation medium results in the physical separation of the tagged amplification product from the non-tagged amplification product (page 240, subheading "Generation of ssDNA").

Mitchell teaches detection of the amplification products (see page 240, figure 1) as well as collection of the amplification products (page 240, subheading "Generation of ssDNA").

Mitchell does not teach separation of the biotin labeled strand from the unlabeled strand using liquid chromatographic reagents, such as organic solvent mobile phases.

Gjerde teaches a method for separating the complementary single-stranded polynucleotide products from one another (see figure 30 and column 39, line 50 to column 40, line 3)

by use of an Matched Ion Pair Chromatography column with nonpolar separation surfaces (see column 12, line 2) which may include silica materials that are derivatized and can be monoliths , including polymeric monoliths as well as beads which may have polymeric surfaces (see column 30, lines 5-49 and column 39, line 50 to column 40, line 3)

and wherein the mobile phase is composed of a variety of different possible components (see column 17, lines 20-60 and column 18, lines 14-25) including organic solvents such as acetonitrile (see column 18, line 24 and column 39, line 60) and a counterion which may include triethylammonium acetate (see column 39, line 59 and column 17, lines 35-60) as well as tributylammonium acetate (see column 17, line 50).

Gjerde teaches that the media and surfaces are free from multivalent cations (abstract). Gjerde teaches the use of beads which fall within the size range claimed (see column 36, lines 47-49). Gjerde teaches treatment of the medium with a

multivalent cation binding agent (see claim 32) as well as acid washing to remove contaminants (see claim 31).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the MIPC separation method of Gjerde to separate the strands as desired by Mitchell since Gjerde states "Liquid chromatography (LC) is a powerful technique for the separation of nucleic acids due to its high resolving capability, short analysis time, and ease of recovery of DNA fragments for subsequent studies. The WAVE.RTM. System combines the precision of ion-pair reversed-phase LC with automated sampling, data acquisition and reporting functions. Fragments can easily be collected and used in downstream experiments such as subcloning, amplification and sequencing. (column 36, lines 20-28)". Thus, an ordinary practitioner would have been motivated to separate the strands as motivated by Mitchell (see abstract) using the method of Gjerde since Gjerde states that the Liquid chromatography method has superior resolution, reduced time and ease of fragment recovery.

7. Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitchell et al (Anal. Biochem. (1989) 178:239-242) in view of Gjerde et al (U.S. Patent 5,772,889) (which is prior art under 102(b)).

Mitchell teaches a method for separating the complementary single-stranded polynucleotide products of an amplification reaction from one another (page 240, subheading "Generation of ssDNA") comprising:

(a) amplifying a target polynucleotide by PCR using two oligonucleotide primers where one primer comprises a biotin tag (which is negatively charged), to produce an amplification product where one strand is tagged with biotin and the complementary strand is not tagged with biotin (see page 240, subheading "PCR amplification"),

(b) applying the amplification product mixture to a separation medium, here streptavidin agarose, wherein the biotin chemical tag can interact with the separation medium (see page 240, subheading "generation of ssDNA").

(c) eluting the amplification products from the separation medium by means of a mobile phase, here the NaOH denaturation step, wherein the interaction between the tag and the separation medium results in the physical separation of the tagged amplification product from the non-tagged amplification product (page 240, subheading "Generation of ssDNA").

Mitchell teaches detection of the amplification products (see page 240, figure 1) as well as collection of the amplification products (page 240, subheading "Generation of ssDNA").

Mitchell does not teach separation of the biotin labeled strand from the unlabeled strand using liquid chromatographic reagents, such as organic solvent mobile phases.

Gjerde teaches a method for separating PCR products (see column 15, example 4)

by use of an Matched Ion Pair Chromatography column with nonpolar separation beads of a diameter of 1-100 microns which are alkylated nonporous polymer beads

(see column 6, lines 17-20) which may be silica polymers that include hydrophobic surfaces (see column 8, lines 1-18 and column 12, lines 1-35)

and wherein the mobile phase is composed of a variety of different possible components (see column 12, lines 38-47) including organic solvents such as acetonitrile (see column 15, line 3) and a counterion which may include triethylammonium acetate (see column 12, line 48) as well as tributylammonium acetate (see column 12, line 47).

Gjerde teaches that the media and surfaces are free from multivalent cations (abstract). Gjerde teaches treatment of the medium with a multivalent cation binding agent (see column 16, example 5) as well as acid washing to remove contaminants (see column 14, lines 35-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the MIPC separation method of Gjerde to separate the strands as desired by Mitchell since Gjerde states "It is an object of the present invention to achieve optimum peak separations during the separation of nucleic acids (column 4, lines 48-50). Gjerde further notes "The invention is a system and method for separating nucleic acid fragments whereby the effects of metal contamination are avoided. (column 4, lines 59-61). Thus, an ordinary practitioner would have been motivated to separate the strands as motivated by Mitchell (see abstract) using the method of Gjerde since Gjerde states that the Liquid chromatography will yield optimal separations while minimizing the effects of metal contamination.

Response to Arguments

8. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection prompted by the IDS.

Conclusion

9. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on June 19, 2002, prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

July 25, 2002